IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

TALECRIS BIOTHERAPEUTICS, INC. and BAYER HEALTHCARE LLC, Plaintiffs, v. BAXTER INTERNATIONAL INC. and BAXTER HEALTHCARE CORPORATION, Defendants.	C. A. No. 05-349-GMS JURY TRIAL DEMANDED **PUBLIC VERSION**
BAXTER HEALTHCARE CORPORATION, Counterclaimant, v. TALECRIS BIOTHERAPEUTICS, INC. and BAYER HEALTHCARE LLC, Counterdefendants.	

REPLY BRIEF OF DEFENDANTS BAXTER INTERNATIONAL INC. AND BAXTER HEALTHCARE CORPORATION IN SUPPORT OF THEIR MOTION FOR LEAVE TO FILE AMENDED ANSWER AND COUNTERCLAIM

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I. Introduction

Crucial experimental data from the laboratory of Dr. William Alonso was withheld from the United States Patent and Trademark Office ("PTO"). Defendants did not know this – and could not have known it – until after discovery was undertaken in this case. Plaintiffs Talecris Biotherapeutics, Inc. and Bayer Healthcare LLC (collectively, "Bayer"), revealed this information only after the date for filing amended pleadings without leave of court already had passed. Defendants Baxter International Inc. and Baxter Healthcare Corporation (collectively, "Baxter"), analyzed the over 125,000 pages of documents disclosed by Bayer and took the depositions of the named inventor, other scientists in his lab, and the prosecuting patent attorneys, to determine whether Bayer truly had suppressed material information. It had, in fact, done so.

Bayer argues that Baxter has not shown good cause for leave to amend because certain other allegations regarding inequitable conduct were publicly available before discovery commenced in earnest. Plaintiffs do not dispute, however, that Baxter could not have discovered the facts regarding the Alonso experiments any sooner. Having learned and then verified these facts during discovery, Baxter promptly sought leave of court to add the defense and counterclaim of inequitable conduct. Baxter has acted responsibly and diligently. Its proposed claim has merit. Bayer will not suffer legal prejudice by allowing this claim to be tested. Therefore, Baxter has shown sufficient "good cause" that the Court should grant its motion to amend.

II. Baxter Has Demonstrated Good Cause For Granting Leave to Amend

Bayer argues that Baxter has failed to show "good cause" for leave to amend under Fed. R. Civ. P. 16(b), ignoring that the absence of undue delay or legal prejudice established by Baxter in its opening brief *de facto* establishes "good cause" under Rule 16(b). *Enzo Life*

Sciences, Inc. v. Digene Corp., 270 F.Supp.2d 484, 490 (D. Del. 2003) ("Given that the Court has already determined that there was no undue delay or a likelihood of prejudice to Enzo [while performing the Rule 15 analysis], the Court concludes that Digene has satisfied the 'good cause' requirement of Rule 16, and accordingly, the Motion to Amend [to add inequitable conduct] [] should be granted.").

Enzo is directly on point. There, as here, defendant moved after the close of discovery to amend its answer to include "a defense/counterclaim of inequitable conduct." *Enzo*, 270 F.Supp.2d at 486. In *Enzo*, as here, the parties produced voluminous amounts of information, and the defendant, Digene, could not take the depositions of the inventors until late in discovery. *Id.* There, as here, plaintiffs argued defendant had not demonstrated good cause under Rule 16(b) and had not met the liberal standard of Rule 15 on the basis that Digene had the relevant facts well prior to filing the motion for leave to amend. *Id.* at 487. Deciding to permit the amended pleading, the court noted "that Digene is pleading a new legal theory based on a new set of facts, which were recently confirmed by the depositions of [the inventors]." *Id.* at 489. In addition, the court observed "that since the Rule 9(b) 'pleading with particularity' requirement is implicated with regard to an inequitable conduct claim, Digene was prudent and possibly required to confirm the factual allegations through discovery." *Enzo*, 270 F.Supp.2d at 489 (emphasis added). The court concluded the proposed amendment to add inequitable conduct was not futile, because "the Court [could] not conclude with certainty, at this juncture, that Digene can 'prove no set of facts in support of [its] claim which would entitle [it] to relief,' given that it has alleged misrepresentations about things such as the effective filing date and mischaracterizing and withholding prior art." *Id.* at 490, *quoting Conley v. Gibson*, 355 U.S. 41, 45-46, 78 S.Ct. 99, 2 L.Ed.2d 80 (1957). Thus, the court concluded that Digene had met the

standards for amending its pleadings under Rule 15 and, therefore, also had met the "good cause" standard under Rule 16(b):

> Further, the Court concludes that Digene filed its amendment soon after it was able to satisfy the pleading requirements of Rule 9(b). Given that the Court has already determined that there was no undue delay or a likelihood of prejudice to Enzo, the Court concludes that Digene has satisfied the "good cause" requirement of Rule 16, and accordingly, the Motion to Amend (D.I.83) should be granted.

Id. (emphasis added).

Baxter, just like defendant in *Enzo*, has clearly met the standards of Rule 15 for amending its pleadings. And, just like this court ruled in *Enzo*, Baxter has also shown sufficient "good cause" to satisfy Rule 16(b) because Baxter has established "there was no undue delay or likelihood of prejudice [to Bayer]."

A. The Suppressed Experimental Results Were Highly Material

The patent-in-suit ("the '191 Patent") would not have issued but for the assertion by Dr. William Alonso and his attorneys that his experiments led to "unexpected" results. Specifically, when appealing the Patent Examiner's refusal to allow the patent, Bayer's lawyer represented to the Board of Patent Appeals and Interferences that the increase in anti-complement activity ("ACA") which is "caused by the TNBP step in step (a) [the solvent-detergent step] ... requires [an incubation step] to reduce the ACA to a level acceptable for intravenous administration." Declaration of Brian T. Clarke In Support of Defendant Baxter International Inc. and Defendant/Counterclaimant Baxter Healthcare Corporation's Motion for Leave to File Amended Answer and Counterclaim, D.I. 167 ("Clarke Decl."), Ex. 4, pg. 4 (emphasis added). And Bayer admits this statement is material, acknowledging to the PTO that "if there is no such increase [in ACA from step (a)] then... the invention itself is not needed." *Id.*, pg. 3. REDACTED

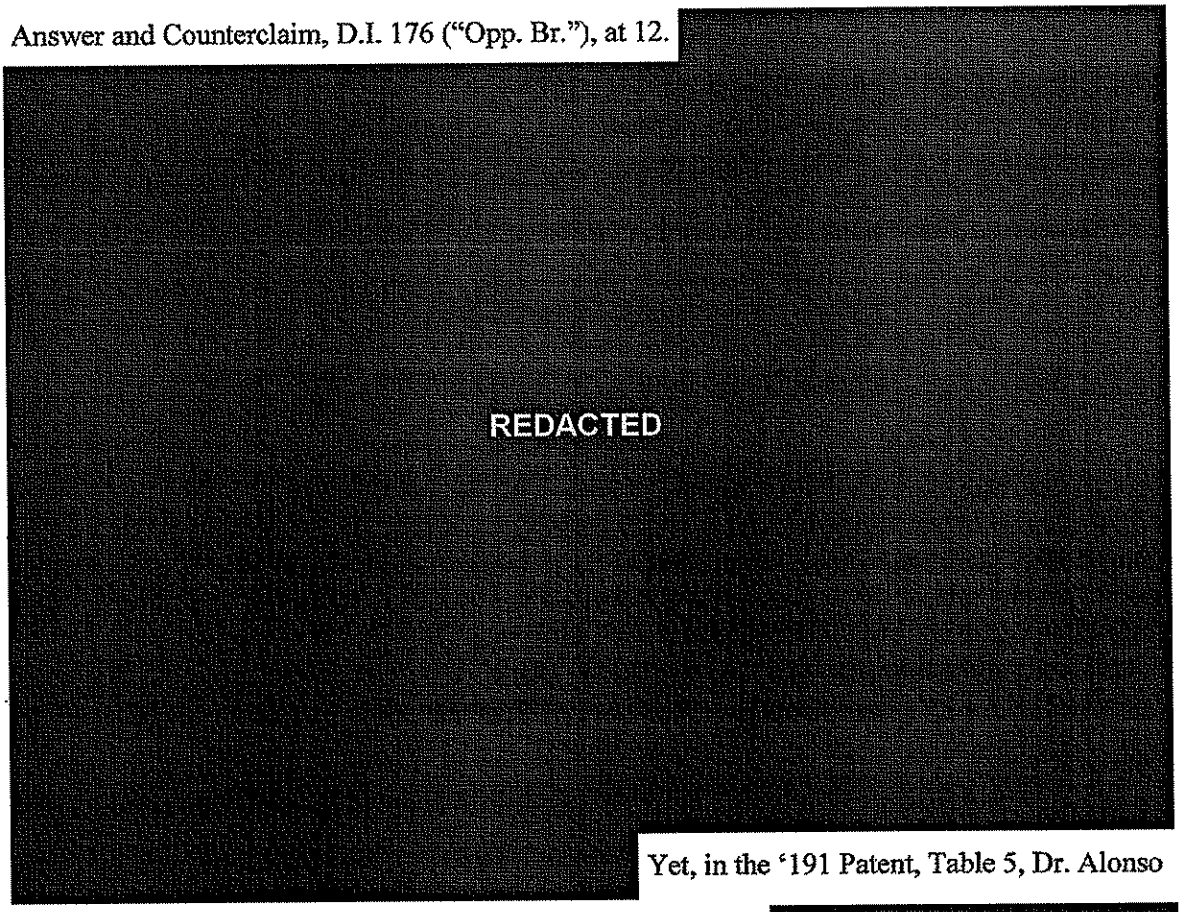
REDACTED Consequently, no "unexpected" or "anomalous" result was obtained, and no incubation step was needed.[1]

REDACTED Consequently, this experimental data clearly was material to patentability.

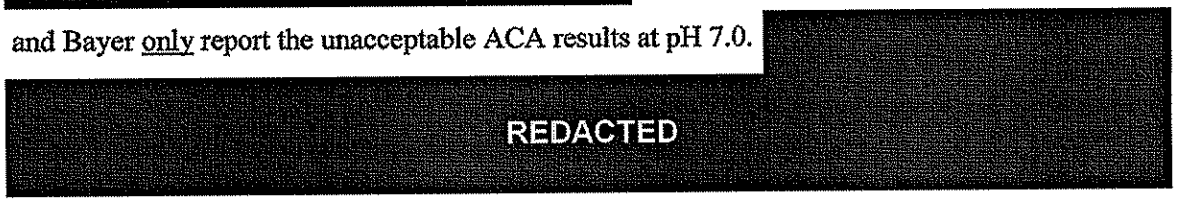
On the last page of its Opposition Brief, Bayer half-heartedly addresses the undisclosed test results. REDACTED Rather, Bayer incorrectly argues the relevance of this data depends on claim construction. It does not. REDACTED It did not increase at all. This is highly material information that should have been disclosed, regardless of how the claims are construed.

[1] Alternatively, it is the cholate that raises ACA, not TNBP.

Bayer also argues, quite disingenuously, that "the pH 5.8 data is cited in the specification." Plaintiffs' Brief in Opposition to Defendants' Motion for Leave to File Amended Answer and Counterclaim, D.I. 176 ("Opp. Br."), at 12.



Yet, in the '191 Patent, Table 5, Dr. Alonso and Bayer only report the unacceptable ACA results at pH 7.0.



B. Bayer Was Obliged to Disclose The Tsay And Ng References

Bayer argues that Dr. Alonso did not have a duty to disclose to the Patent Office the Ng *et al.* and Tsay references, because these references were cumulative of, or less material than, the

Tenold reference already of record. The duty of candor requires patent applicants[2] to disclose to the PTO information material to the patentability of the invention. *GFI, Inc. v. Franklin Corp.*, 265 F.3d 1268, 1274 (Fed. Cir. 2001), *citing Halliburton Co. v. Schlumberger Tech. Corp.*, 925 F.2d 1435, 1440 (Fed. Cir. 1991); *see also* 37 C.F.R. § 1.56(b). While this duty does not require an applicant to disclose "an otherwise material reference to the PTO if that reference is merely cumulative or is less material than other references already before the examiner," *id.*, the Ng *et al.* and Tsay references are not merely cumulative of, or less material than, Tenold.

The inventor, Dr. Alonso, argued *in the patent itself* that Tenold does not disclose a viral inactivation step. Clarke Decl., Ex. 1 ,Col. 10:1-3 ("The Tenold '608 method omits the viral inactivation step…."). The first step of claim 1 of the '191 patent to Dr. Alonso involves viral inactivation using a trialkylphosphate and a detergent. Thus in stating that Tenold did not disclose a viral inactivation step, Dr. Alonso was arguing that Tenold did not teach a limitation of the claims. In contrast, Tsay and Ng *et al.* each disclose a viral inactivation step using a trialkylphosphate and a detergent. Reply Declaration of Brian Clarke in Support of Motion for Leave to Amend (hereafter "Clarke Reply Decl.") Ex. 1, p. 82; Clarke Reply Decl.,Ex. 2, Col. 13:55-14:11. For this reason alone, Tsay and Ng *et al.* cannot be cumulative or less material art than Tenold, as Bayer now implausibly urges. Therefore, the law required Dr. Alonso and his counsel to disclose these material references to the Patent Office.

During prosecution, Dr. Alonso argued that "Tenold did not teach how to obtain a decrease in ACA." Clarke Decl. Ex. 7, p. 5. In direct contrast to Dr. Alonso's characterization of Tenold, both Tsay and Ng *et al.* describe incubating antibody solutions, previously treated

[2] "Patent applicant" includes all those under the duty of candor pursuant to 37 CFR § 1.56.

with solvent-detergent to inactivate viruses, to reduce non-specific complement activation, *i.e.*, anticomplement activity. Clarke Reply Decl. Ex. 1, p. 82; Clarke Reply Decl., Ex. 2, Col. 13:55-14:11. Indeed, even the title of the Tsay reference, "Heat Treatment of IgM-Containing Immunoglobulins to Eliminate Non-Specific Complement Activation," directly indicates the reduction of ACA by incubation. The reduction of anticomplement activity by incubation is, of course, material to the patentability of the claims because step (b) of claim 1 recites "incubating the solution of step a) … such that the increased anticomplement activity of the solution is reduced…." Again, Tsay and Ng *et al.* cannot be cumulative or less material art than Tenold because, at a minimum, Tsay and Ng *et al.* describe steps of the claims that Dr. Alonso argued, both during prosecution and in the specification, Tenold does not teach. A cumulative or less relevant reference provides the same or very similar teachings as references already of record with the Patent Office, which is why the rules do not require disclosure of such references. However, both Ng *et al.* and Tsay teach elements of the invention claimed by the '191 patent, which elements Dr. Alonso and/or his representatives both argued Tenold did not teach or suggest.

Grasping at straws, Bayer argues that Baxter's designation in foreign proceedings of Tenold as the "closest prior art" for its inventive step challenge in Europe, followed by its later designation of Ng *et al.* as the closest prior art, somehow means that in the United States the Ng *et al.* reference is less material than Tenold. Baxter, in its European opposition to the foreign counterpart of the '191 patent, argued that the European patent[3] lacked an inventive step[4] over

[3] The claims of the European patent differ from the claims of the U.S. patent but, in Baxter's opinion, also are not valid. Indeed, Bayer has now entered a consent order that its patent in the United Kingdom be revoked and is invalid. Clarke Reply Decl., Ex. 3.

the prior art. In European prosecution or opposition proceedings an examiner or an attorney will make the case for or against inventive step by first identifying a prior art disclosure as "the closest item of prior art," which prior art will serve as a point of reference for comparison to additional prior art references to determine whether the combination provided an obvious solution to the problem solved by the invention. Clarke Reply Decl. ¶ 6. It is accepted practice in an opposition to switch from one combination of references to a different combination of references when arguing lack of inventive step.[5] *Id.* ¶ 7. Hence, when there is more than one combination of references, the accepted practice in Europe often necessitates switching the designation of the closest prior art from one of the references in the first combination to one of the references in the second combination. *Id.* ¶ 8. Changing the designation of the closest prior art from one reference to another does not inform the reader about the relative materiality of the two references; it is merely a procedural device to facilitate discussion of a particular combination of references for making an inventive step determination in Europe. *Id.*, ¶ 9.

Thus, the Ng *et al.* and Tsay references are not cumulative references to Tenold or any other reference of record with the Patent Office. Both Ng *et al.* and Tsay teach key elements of the invention claimed in the '191 patent, which elements Dr. Alonso argued were missing from the references of record, particularly from the Tenold reference. Consequently, these references should have been disclosed to the PTO examiner by the applicant and his attorneys during

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[4] In Europe the lack of an inventive step is analogous, but not identical, to obviousness under U.S. Patent law.

[5] For example, if the claimed invention provides a process that is said to produce a product in high yield and high purity, one prior art reference might disclose a similar process in which the yield was high but the purity was low, such that the "problem" was to increase purity; whereas another reference might disclose a similar process in which the product was pure but obtained only in a low yield, such that the "problem" was to increase the yield. Thus, each reference could justifiably be designated the "closest item of prior art," depending upon which aspect of the claimed invention was being analyzed.

prosecution of the '191 patent.

C. Bayer Did Not Disclose That Its Own Product, Gamimune N, Anticipated Claim 23

Bayer's Gamimune® N product, which was on sale more than one year before the '191 patent application was filed, has product characteristics that appear to meet all the limitations in Claim 23. Dr. Alonso and/or Bayer, however, did not disclose the formulation of this product to the PTO. Rather, they made only a general reference to the product in the patent, and now Bayer argues this was sufficient to disclose to the Patent Office the underlying properties of the Gamimune® N product that were material to the patentability of the invention claimed in the '191 patent.

A patent applicant must disclose "*any* information that a reasonable examiner would be substantially likely to consider important in deciding whether to allow an application to issue as a patent." *GFI, Inc.*, 265 F.3d at 1274 (emphasis in original); *accord Liquid Dynamics Corp. v. Vaughan Co., Inc.*, 449 F.3d 1209, 1226 (Fed. Cir. 2006). Dr. Alonso knew that his employer, Bayer, manufactured an intravenously injectable immune serum globulin solution called "Gamimune N" that was substantially free of lipid enveloped viruses, had a low ionic strength, a pH between about 3.5 and about 5.0, an antibody concentration of about 10% wt./wt. and a glycine concentration of about 0.2M, as required by Claim 23. However, nowhere in the specification does Dr. Alonso provide the examiner with the information for Gamimune N that "a reasonable examiner would . . . substantially likely . . . consider important in deciding whether to allow an application to issue as a patent." *Id.* Bayer and Dr. Alonso provided only the following information relating to Gamimune N in the specification (also cited by Bayer in its opposition brief, Opp. Br. at 11):

> The 5% formulation (5% IGIV) is made tonic by the addition of 10% maltose. The 10% formulation contains 0.2 M glycine in order to achieve an isotonic preparation without large quantities of sugar. The product with either formulation (Gamimune®N 5% or Gamimune®N 10%) experiences shifts in molecular distribution (antibody aggregation) when the ionic strength of the low pH solution is increased. Therefore, sodium chloride, which is often used to achieve tonicity, should not be used.

Clarke Decl., Ex. 1, Col. 5:33-40.

Bayer asserts, *ipsit dixit,* that this was "more than sufficient disclosure," because the word Gamimune includes the registered trade mark symbol ®, thereby indicating the product is sold in commerce. Opp. Br. at 11. That is wrong. Trademarks already registered overseas by foreign companies such as Bayer A.G. need not be used in commerce in the United States in order to be registered here. 15 U.S.C. §1126(e). Moreover, the Manual of Patent Examination Procedures specifies that trademarks ordinarily do not constitute sufficient disclosure of "positive, exact, intelligible" characteristics of a product. MPEP, § 608.01(v)(1). Consequently, a patent applicant has not disclosed material prior art by mere recitation of a trademark in a patent application. *White Consol. Indus., Inc. v. Vega Servo-Control, Inc.*, 713 F.2d 788, 790 (Fed. Cir. 1983). Burying the name of a product in a patent application does not disclose the characteristics of that product such that an examiner can compare the disclosed product's characteristics with the claimed invention to determine "whether to allow an application to issue as a patent." *GFI, Inc.*, 265 F.3d at 1274. Unlike scholarly articles or issued patent applications, the chemical composition of a proprietary product is not information readily available to a patent examiner.

The cases cited by Bayer do not support its argument that reciting the tradename Gamimune N is sufficient disclosure to meet the duty of candor. In *Ruiz v. A.B. Chance Co.*, 234 F.3d 654 (Fed. Cir. 2000) the Federal Circuit considered a patent involving underpinning (supporting) the foundations of residential and commercial buildings. *Ruiz*, 234 F.3d at 660.

The defendants in *Ruiz* argued to the district court, as summarized by the Federal Circuit, that "Chance failed to properly disclose the use of screw anchors as taught in the [prior art] Fuller and Rupiper methods." *Id.* at 670. The Federal Circuit also summarized the district court's findings: "The district court found that the screw anchor language was properly disclosed in the specification of the '368 and '107 patents." The Federal Circuit then went on to quote the district court's conclusion:

> The district court said, 'the earth anchor language in the specification combined with the reference to a piling and other materials in the patent file wrapper history are sufficient to disclose the Fuller and Rupiper prior art.'

Id.

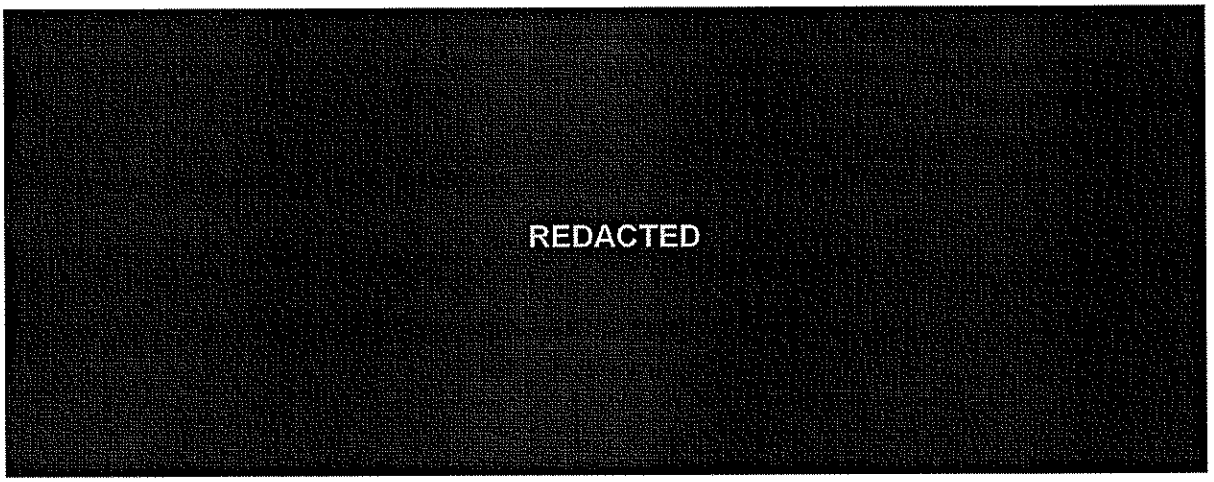
Bayer mischaracterizes this passage of the opinion as indicating that the specification in the *Ruiz* case only "disclosed 'earth anchor language' and a 'reference to a piling and other materials in the patent file wrapper history.'" Opp. Br. at 11, *quoting Ruiz*, 234 F.3d at 670. Bayer asserts that the Federal Circuit's summary of the patent-in-suit's disclosure was "'sufficient to disclose. . . the prior art,'" and "[f]or the same reason, the '191 specification's explicit disclosure of Gamimune®N 10% is more than sufficient disclosure of prior use." *Id.* In fact, however, the full text of the Federal Circuit opinion reveals that the district court reviewed the file history and found within it sufficient disclosure of the prior art. Here, in contrast, Bayer has not pointed to anything in the file history (or the specification) disclosing the actual characteristics of the Gamimune N product sufficient to constitute adequate disclosure to the PTO.

Bayer also cites the nonprecedential opinion, *Bayer AG v. Housey Pharms., Inc.*, 128 Fed. Appx. 767 (Fed. Cir. 2005), as support for its untenable position that the mere disclosure of a registered trade name in a patent application meets an applicant's obligation to disclose

information material to patentability. In *Bayer AG,* the patentee specifically disclosed two prior art references within the specification. *Id.* at 770. The district court held and the Federal Circuit affirmed the unremarkable proposition that disclosure of specific scientific articles in an application is sufficient disclosure to avoid a claim of inequitable conduct.

No amount of hand waving can turn the passing reference to a registered trade name in an application into a disclosure of material information that "a reasonable examiner would . . . substantially likely . . . consider important in deciding whether to allow an application to issue as a patent." *GFI, Inc.*, 265 F.3d at 1274. In full candor, Bayer should have explicitly disclosed to the PTO the composition of the product it already was selling.

III. Baxter Did Not Delay Seeking Leave to Amend



To confirm the significance of this data, and that it was known by the lawyers who prosecuted the patent application, Baxter took the depositions of James Giblin, Mary Boguslaski and Christine Hansen, the '191 patent's prosecuting attorneys, Susan Trukawinski, a scientist in Dr. Alonso's lab, and the applicant, Dr. Alonso. Those depositions were not concluded until

early October, 2006[6]; Baxter filed this motion less than thirty days later.

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Similarly, Baxter did not learn the specifics of the formulation of Gamimune N and the process for manufacturing it until reviewing in detail Bayer's documents.

Plaintiffs suggest that Baxter should have filed two motions for leave to amend – one after discovering the Tsay and Ng references (Opp. Br. at 5-6) and, presumably, the other after discovering the suppressed experimental data. The law does not require such pointless inefficiency; Baxter marshaled multiple bases for its claim of inequitable conduct and properly has presented all of them together in one proposed new pleading.

IV. Bayer Has Not Been Prejudiced

Plaintiffs' only assertion of potential prejudice is that Grace Tsay and Paul Ng, the authors of the undisclosed references, already have had their depositions taken. Opp. Br. at 8. That fact will not cause Bayer any harm. The relevance of the published references is what they say on their face – the documents "speak for themselves." And Paul Ng is represented by counsel for plaintiffs so is available to them as needed. Clarke Reply Decl., ¶ 22. Moreover, the prosecuting attorney, James Giblin, a former Bayer employee (Clarke Reply Decl., Ex. 9, pp. 9

[6] Baxter asked to take the depositions of Susan Trukawinski and William Alonso early in discovery but Talecris pushed these depositions out until late September. Clarke Reply Decl., Exs. 4 and 5.

and 12) is represented by counsel for Bayer. Allowing amendment at this time will not prejudice Bayer's ability to defend against the counterclaim at trial.

V. Conclusion

Leave to amend "shall be freely given" when, as here, justice so requires. *Foman v. Davis*, 371 U.S. 178, 181-82 (1962). Because it has presented a valid claim in a timely fashion, Baxter's request for leave to add an affirmative defense and counterclaim of inequitable conduct should be granted.

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CERTIFICATE OF SERVICE

I, Philip A. Rovner, hereby certify that on December 4, 2006, the within document was filed with the Clerk of the Court using CM/ECF which will send notification of such filing(s) to the following; that the document was served on the following counsel as indicated; and that the document is available for viewing and downloading from CM/ECF.

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